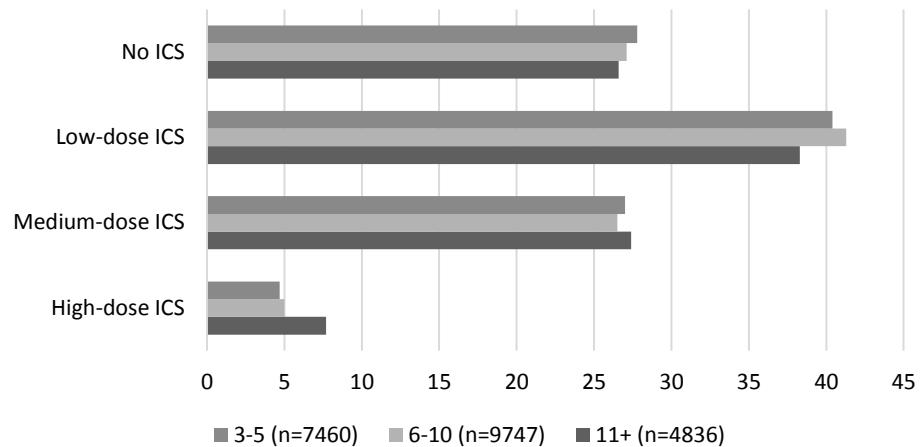


Supplementary data

Figure S1. Proportion of patients on ICS therapy in different SABA overuse groups, according to continuous overuse of SABA during the baseline year (top panel) and after 3 years follow-up (lower panel)

ICS and SABA use during baseline year



ICS and SABA use during year 3

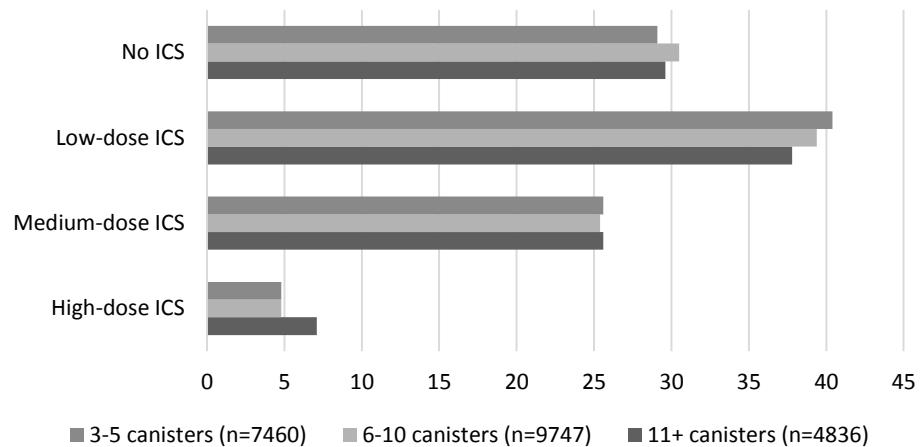


Table S1. Definition of treatment steps

| Treatment step | Definition |
|----------------|--|
| Step 0 | - No dispensing of SABA, LABA, LTRA or ICS |
| Step 1 | - SABA monotherapy |
| Step 2 | - Low-dose ICS - LTRA monotherapy |
| Step 3 | - Medium-/high-dose ICS - Low-dose ICS + LABA or LTRA |
| Step 4 | - Medium-/high-dose ICS + LABA - Medium-/high-dose ICS + LABA or tiotropium - Medium-/high-dose ICS + LTRA |
| Step 5 | - Continuous use of oral steroids (OCS)* - Continuous use of anti-IgE or anti-IL5 |

*Equivalent to a cumulative dosage of ≥ 1000 mg prednisolone per year

Table S2. SABA and ICS use during study period

| | Baseline year (n=365,324) | Follow-up year 1 (n=365,324) | Follow-up year 2 (n=365,073) | Follow-up year 3 (n=334,847) |
|----------------------------------|--------------------------------------|---|---|---|
| SABA canisters, n (%) | | | | |
| 0-2 | 254,500 (69.7%) | 301,413 (82.5%) | 306,849 (84.1%) | 283,385 (84.6%) |
| 3-5 | 76,619 (21.0%) | 41,846 (11.5%) | 37,540 (10.3%) | 32,589 (9.7%) |
| 6-10 | 27,065 (7.4%) | 16,575 (4.5%) | 15,304 (4.2%) | 13,861 (4.1%) |
| 11+ | 7140 (2.0%) | 5490 (1.5%) | 5380 (1.5%) | 5012 (1.5%) |
| ICS dose, n (%) | | | | |
| No ICS | 100,587 (27.5%) | 203,484 (55.7%) | 214,575 (58.8%) | 205,755 (61.4%) |
| Low dose | 149,925 (41.0%) | 94,964 (26.0%) | 90,310 (24.7%) | 79,185 (23.6%) |
| Medium dose | 98,449 (26.9%) | 57,820 (15.8%) | 51,987 (14.2%) | 43,126 (12.9%) |
| High dose | 16,363 (4.5%) | 9,056 (2.5%) | 8,201 (2.2%) | 6,781 (2.0%) |

Table S3. Risk of exacerbation after baseline period stratified by history of exacerbation during baseline period

| | Crude HR (95% CI) | P value | Adjusted HR (95% CI) | P value |
|------------------------------------|----------------------|---------|-------------------------|---------|
| No exacerbation at baseline | | | | |
| Baseline SABA use | | | | |
| ≤2 canisters | 1.00 | | 1.00 | |
| 3-5 canisters | 1.16 (1.14-1.18) | <0.001 | 1.20 (1.18-1.22) | <0.001 |
| 6-10 canisters | 1.34 (1.31-1.37) | <0.001 | 1.33 (1.30-1.36) | <0.001 |
| 11+ canisters | 1.72 (1.65-1.79) | <0.001 | 1.62 (1.55-1.69) | <0.001 |
| Exacerbation at baseline | | | | |
| Baseline SABA use | | | | |
| ≤2 canisters | 1.00 | | 1.00 | |
| 3-5 canisters | 1.21 (1.18-1.24) | <0.001 | 1.19 (1.16-1.22) | <0.001 |
| 6-10 canisters | 1.37 (1.32-1.42) | <0.001 | 1.33 (1.29-1.38) | <0.001 |
| 11+ canisters | 1.60 (1.51-1.69) | <0.001 | 1.53 (1.45-1.61) | <0.001 |

Adjusted for treatment step (GINA 2018), gender, age, and Charlson Comorbidity Index.